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PYEMIA DUE TO AN ANAEROBIC POLYMORPHIC BACILLUS, PROBABLY BACILLUS FUSIFORMIS.*

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(From the Memorial Institute for Infectious Diseases.)

The Bacillus fusiformis, the anaerobic organism found so frequently in pathological lesions, nearly always occurs in conjunction with aerobic bacteria and some authors even question its pathogenicity. The following case is reported because, so far as we can determine, it is the first fatal general infection caused by this bacillus alone.

The essential facts of the clinical history are as follows:

The patient, a middle-aged man, died from pyemia following an attack of appendicitis. Early operation was refused. An operation five weeks later by Dr. Bevan, to whom we are indebted for the opportunity to make this study, revealed a small pericecal abscess containing a sloughed appendix. Drainage at this time failed to check the septic temperature which the patient had had for some time previously and which continued until death six weeks later. Repeated blood examinations showed a leukocytosis of from 14,000 to 22,000. Three blood cultures were negative. Of these the third was kept under anaerobic conditions. A number of needle punctures of the liver failed to show liver abscess. One month before death metastatic abscesses began to appear over the thigh and tibia and two weeks before death the patient coughed up a large amount of a foul smelling pus.

Anatomic diagnosis (Dr. Rosenow).— Retroperitoneal and retrocecal abscess; thrombophlebitis of contributory retroperitoneal veins; multiple pulmonary infarction with abscess formation; multiple metastatic suppurative periostitis and osteomyelitis; acute pleuritis; infarct of spleen; adhesive localized pleuritis and peritonitis;

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fatty infiltration of liver with passive congestion. The examination was made three hours after death. The following statements taken from the postmortem record cover the important points: The peritoneal cavity is free from fluid. The lateral and posterior portion of the cecum is bound firmly to the abdominal wall by fibrous adhesions. The stump of the appendix has entirely healed. On tearing the parietal peritoneum and adhesions along the posterior and outer aspect of the cecum there is opened an abscess from which exudes approximately 200 c.c. of a whitish-yellow, thick, intensely fetid pus. The wall of the abscess is irregular and ragged, easily torn, and contains a number of pockets filled with a similar pus.

On section of the tissues behind and to the left of the abscess a number of veins are cut across which are filled with adherent clots. No evidence of portal thrombosis is found.

The spleen is enlarged, soft, and contains a light-colored, wedge-shaped area (2×2×1 cm.) surrounded by a hyperemic zone.

The liver shows a moderate infiltration of fat and passive congestion.

The left pleural cavity is free from fluid. Fibrous adhesions are bound over two medium-sized, wedge-shaped areas on the left upper lobe and over the greater part of the lower lobe. The latter is the seat of a large abscess, containing approximately 500 c.c. of a blood-stained, chocolate-colored, intensely fetid pus. The inner and anterior walls are ragged, irregular, and surrounded by compressed lung, while the lower wall is largely made up of diaphragm. Two wedge-shaped areas of the left upper lobe show softening in the center and are filled with foul smelling pus. An abscess corresponding to the one in the left lower lobe is found just above the diaphragm in the right lower lobe and contains fully 300 c.c. of a similar pus. Four wedge-shaped areas like those found in the left upper lobe are found in the right lung. Cross-section at the apex of some of these areas shows one or more veins filled with adherent clots. No direct communication between the abscesses of lungs and the retrocecal abscess was found.

The stomach, intestines, mesenteric lymph-glands, kidneys, adrenals, pericardium, endocardium, and myocardium show no noteworthy changes.

Microscopic examinations of sections of the wall of the large abscess shows it to consist of necrotic tissue surrounded by granulation tissue and compressed lung, infiltrated with leukocytes. The wedge-shaped areas consist of a central necrotic material surrounded by a hyperemic zone with infiltration of leukocytes.

The liver shows a marked fatty infiltration, a definite increase in interstitial tissue, and passive congestion. No noteworthy change was found in the rest of the organs.

Bacteriology.— Microscopic examination of stained smears of the pus obtained from the abscess of the tibia before and after death, from the large abscess in the left lung, and the retrocecal abscess after death, and from infarcts shows slender, spindle-shaped bacilli, with pointed ends, varying greatly in length (3 to 40 μ). They often occur in large masses of long, wavy filaments, twisted together in ropelike fashion and as short spirals (Plate 1, Fig. 1). The twisted threads at times extend across a number of fields of

the oil immersion lens. The ends are usually tapering and curled upon themselves. The threads are undoubtedly made up of many bacilli because at times distinct evidence of a break in angle occurs at the junction of each bacillus. Many small coccus forms are found singly, in pairs, and often in clumps of 50 or more. The masses of cocci are often found near or within the entangled masses of bacilli, while single cocci and diplococcus forms are not infrequently observed near or within a widened portion of the long filaments or single bacilli. There seem to be breaks in one side of these enlarged ends and here the small coccus forms seem to escape.

The pus from the right lung shows the presence of a large number of the same bacilli and coccus forms and in addition a large gram negative bacillus entirely different from those described and which we regard as a contamination, since rupture of the abscess had taken place during life.

No definite motility can be made out although vibratory motion of the ends of the long filaments is seen. The small coccus forms and bacilli are largely decolorized when treated by Gram's method. The bacilli stain with difficulty and the more penetrating stains such as carbol-gentian-violet or carbol-fuchsin are necessary to bring them out clearly.

The fusiform bacillus was isolated in pure culture by growing it anaerobically (Wright's pyrogallic acid method) on slants of blood agar at 37° C. The organism grows on human, sheep, and goat blood agar. Of these the latter is the most favorable medium. The bacillus grows poorly in 0.2 per cent dextrose broth and serum broth. No growth has been obtained on plain agar or Loeffler's blood serum. Growth generally occurs after 48 hours' incubation at 37° C.

The colonies are grayish-white in color, rather shiny, and usually have regular edges. When old, the colonies frequently become indented in the center and flattened at the edges. In early cultures, especially, the colonies are quite adherent to the medium. The colonies vary from the size of a pin-point to 2 mm. in diameter. Single colonies always contain fusiform bacilli and very small gram negative coccus forms which are often in pairs and clumps, just as in the smears from the pus. In the fluid of condensation the

organisms often grow in yellowish-white balls. The blood agar is often colored green, especially near the fluid of condensation.

An offensive odor is given off in successful cultures.

No progressive motion could be observed, but a distinct vibratory motion is seen, especially at one end.

The bacilli die quickly. It is very difficult to get a growth from a single colony, only about one out of 10 such cultures being successful. To assure growth a large amount of pus or culture must be inoculated. It was never possible to separate the coccus forms from the fusiform bacilli or to get growth from colonies containing mostly coccus forms and few bacilli. The coccus forms also grow only in anaerobic cultures which differentiate them from *melitensis* which they resemble. The bacillus is very polymorphous. The forms seen in pure cultures closely resemble those seen in the pus. In the cultures the proportion of bacilli and short spiral forms is generally greater than in the smears made from the pus. In pure culture the organism appears as straight, or slightly bent, pointed bacilli of varying lengths, some being very short, long, wavy filaments, ropes, long and short spiral forms, and coccus forms. The filaments sometimes form a circle, assume U-shapes and occasionally have a curved end. The coccus forms are usually found near the twisted threads and at times are seen inside or escaping from swollen ends, just as seen in the pus. Occasionally they appear in short chains. No spores can be demonstrated in these cultures. Involution forms in a great variety of shapes are sometimes seen in the old cultures. Distinctly spiral forms are seen only in the fluid of condensation in the early cultures, but appeared on the surface of the solid media after six weeks' cultivation. The filaments and spiral forms are often seen to be made up of strings of bacilli as in the smears from the pus (Plate 1, Fig. 1). The spiral forms are best seen in the hanging drop, India ink preparations, and in smears fixed by heat or with methyl alcohol and then stained with carbol-gentian-violet or polychrome methylene blue (24–48 hours). A 10 per cent saturated solution of gentian-violet in 5 per cent phenol was found the most satisfactory stain. It is not necessary to heat the stain. The organisms are not positively stained by Gram's method.

This bacillus corresponds closely, culturally and morphologically, with those isolated in pure culture by Tunnicliff[1] from the normal mouth, noma, membranous angina, and gingivitis. The only differences are the coccus forms, which resemble somewhat the spores described by Tunnicliff, and the cup-shaped colonies in old cultures. Morphologically Tunnicliff's organism is extremely polymorphous, appearing as short bacilli, filaments, long and short spiral forms.

These strains of fusiform bacillus appear to be similar to that of Kasper and Kern.[2] The difference in culture media probably causes greater production of spiral forms in the cultures here described. The predominance of long ropes and filaments in the pus from the internal organs may be due to a greater degree of anaerobiosis than is found in the mouth, in noma, membranous angina, and gingivitis, where short spirilla are observed. The cases of pyemia in which long filaments and ropes are found are much more chronic than cases of noma and Vincent's angina, and the long period of growth in the fluids of the same individual may account for the large number of filaments and long spirals instead of the short forms. This is in accord with the observations of Tunnicliff that the filaments and spirals are a later stage in the development of the fusiform bacillus.

The chronicity of infection in these cases may explain also the greater adherence of the colonies to the surface of blood agar just as Rosenow[3] has shown in cases of chronic pneumococcus endocarditis in which the property of adherence and chain formation is probably the result of long growth in serum rich in agglutinins.

Animal experiments.—The virulence of the microorganism was tested on white rats, rabbits, and guinea-pigs. Two white rats which received four daily intraperitoneal injections of 1 c.c. of pus remained permanently well. Two guinea-pigs which were injected intraperitoneally with 0.5 c.c. of the fresh pus from the left lung died at the end of 48 hours. No gross lesions or bacteria could be found after death. Two guinea-pigs injected repeatedly with the

[1] *Jour. Infect. Dis.*, 1906, 3, p. 148; *ibid.*, 1911, 8, p. 316.

[2] *Centralbl. f. Bakt.*, I, Orig., 1910, 55, p. 97.

[3] *Jour. Infect. Dis.*, 1910, 7, pp. 411, 429.

pus after it was kept on ice for 48 hours and longer remained well. It was thought that repeated injections of the pure culture might be of interest and accordingly two rabbits were injected intraperitoneally with the growth from two to six blood agar slants on successive days. They died in four and 13 days respectively. In one peritonitis was found and the bacillus easily made out in smears from the flakes of fibrin, but the cultures unfortunately remained sterile. In the other no gross lesions were found. A third rabbit having previously received four daily intravenous injections of 1 c.c. of pus was not made noticeably ill by three large doses of the pure culture. It seems as if the injections of the attenuated pus conferred a definite immunity. One rabbit and one guinea-pig, injected subcutaneously with the contaminated pus from the right lung abscess, died in three days. Microscopic and cultural examination of the pus, which had infiltrated the subcutaneous tissue over a large area, proved the presence of a large number of fusiform bacilli together with the gram negative saprophytic aerobic bacillus isolated previously and which proved nonvirulent for a guinea-pig. The small coccus forms described above were found both in the pus and in cultures. No metastatic abscesses could be found anywhere.

Ghon and Mucha,[1] and Kasper and Kern report similar cases where the exact etiological rôle of a similar bacillus, which they believe to be the bacillus fusiformis, is not quite so clear because it was not found in pure culture. Our results appear to show that the bacillus fusiformis by itself may be pathogenic.

EXPLANATION OF PLATE 1.

FIG. 1.—Pus from retrocecal abscess, showing long threads, ropelike twists, short spiral, and coccus forms. Carbol-gentian-violet. ×1,000.

FIG. 2.—Pus from abscess in left lung. Carbol-gentian-violet. ×750.

FIG. 3.—Culture of fusiform bacilli from pus in right lung after 48 hours' growth on goat blood agar. Carbol-gentian-violet. ×750. (The large thick bacillus is a contaminating bacillus from which the cultures of fusiform bacilli were freed later.)

FIG. 4.—Smear showing straight and curved bacilli and spirals from 48 hours' growth on goat blood agar. Carbol-gentian-violet. ×1,000.

[1] *Centralbl. f. Bakt.*, I, Orig., 1909, 49, p. 493.

PLATE 1.

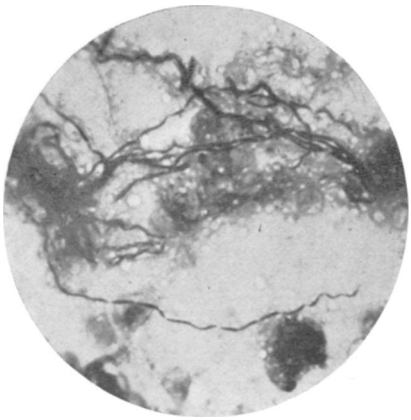

FIG. 1.

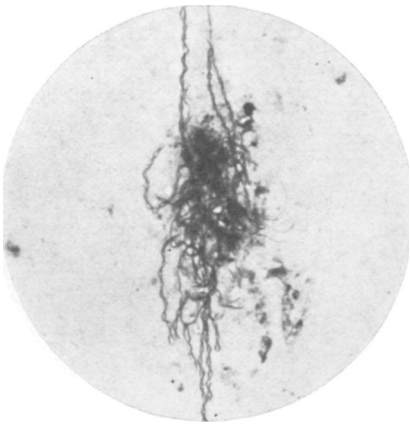

FIG. 2.

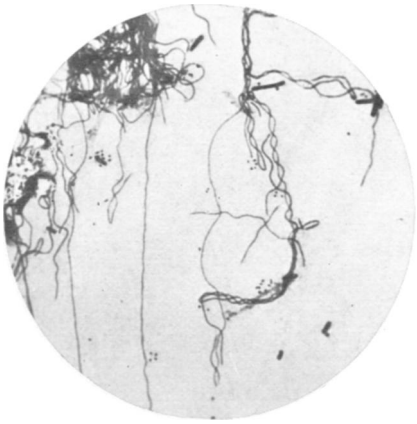

FIG. 3.

FIG. 4.